

The EDMVS' Draft Work Plan

Presentation to the EDMVS,
June 5, 2002

Purpose of Today's WorkPlan

- Show progress of EDSP
- Provide the status of each assay
- Project what's next

Tier I Screening Battery

recommended for consideration by EDSTAC

- Steroidogenesis
- Pubertal - female
- Fish Screen

aka short term fish reproduction

- Amphibian Metamorphosis
- Estrogen / Androgen receptor binding
- Hershberger
- Uterotrophic

Alternative Assays

recommended for consideration by EDSTAC

Tier I

- Aromatase
- Pubertal male
- Adult 14 –day intact male

Tier ?

- In Utero through Lactation

Tier II Assays

recommended for consideration by EDSTAC

- Mammalian 2-generation
- Avian 2-gen. Reproduction
- Amphibian Development and Repro.
- Invertebrate (Mysid) Lifecycle
- Fish Lifecycle

Steroidogenesis (Tier I)

<u>Milestone</u>	<u>Current Status</u>
• DRP/Protocol	✓ June 02
• Prevalidation	
-section testes optimization	Today, Aug 03
-cell based (H295R)	In ORD Lab
• Validation	
-multi-chemical	to lab Aug 03
-inter-lab	to lab Aug 03

✓June 03 = complete, date presented to EDMVS

Pubertals – m&f (Tier I)

<u>Milestone</u>	<u>Current Status</u>
• DRP equivalent	✓ Dec 01
• Prevalidation	
-Single Dose Study	✓ Dec 01
-Multi-chemical & multi-dose Protocols	✓ Dec 01
-Multi-chemical & multi-dose Studies data to EDMVS Aug 03	In lab
-Restricted Feeding Study	✓ July 02
• Validation (inter-lab)	To lab Aug 03

Fish Screen (Tier I)

Milestones

- DRP/Protocol
- Prevalidation

-ShortTerm Fish Repro. in FHM ✓ Mar 02

-Short term fish repro. In
FHM w/multi-chemicals

- Comparative Study Plans:

-Comparative Studies:

Vitellogenin Methods (FHM,
Medaka, Zebrafish)

Fathead Minnow Assays

- Validation (inter-lab)

Current Status

✓ Mar 02

✓ Mar 02

In lab ☺

✓ Mar 02

To EDMVS Aug 03

In lab ☺

In lab ☺

depends on OECD

Amphibian Metamorphosis (Tier I)

formerly Frog Thyroid

Milestone

- DRP/Protocol ✓ July 02
- Pre-validation
 - prometamorphosis protocol demonstration proj. Dec 03
 - optimization studies TBD
- Validation (inter-lab) in 2005
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Current Status

ER / AR binding (Tier I)

ICCVAM

- **Scientific Expert Panel's retrospective validation** **May 2002**
- **Expert Panel Final Report** **Sept 2002**
- **EDMVS Updated by ICCVAM** **July 02**
- **EDSP: AR in lab (prevail)** **Aug 02 – Sept 03**
- **EDSP: ER in lab (validation)** **May 02 – May 04**

Aromatase (Tier I)

Milestones

- DRP / Protocol ✓ Mar 02
- Prevalidation
 - placental microsomal assay Today & Aug 03
 - compare bovine, human, porcine
 - cell based assay Today & Aug 03
 - comparison: microsomal & recombinant & multi chem Today & Aug 03
- Validation (inter-lab) to lab Sept 03

Current Status

In Utero → Lactation (Tier ?)

Milestone

- DRP
 - Protocol review
- Prevalidation
 - Protocol Demo
 - Multi-chem study
- Validation (inter-lab)

Current Status

- ✓Dec 02
- ✓Mar 02
- report due 8/03
- TBD
- TBD

Tier II Assays

Mammalian 2-generation (Tier II)

<u>Milestone</u>	<u>Current Status</u>
• DRP/Protocol	--
• Prevalidation	
One-gen. Ext. Protocol	✓ Dec 02
Propylthiouracil Study	✓ July 02
One-gen Ext. study	Tomorrow
• Validation (inter-lab)	TBD

Avian 2-gen. Reproduction (Tier II)

Milestone

- DRP/Protocol
- Prevalidation
 - Avian Dosing Study Plan
 - Avian Dose Study
 - Protocol demo
- Validation (inter-lab)

Current Status

- ✓ Fall 03
- ✓ Mar 02
in lab
- future
- future

Amphibian Dev. & Repro. (Tier II)

Milestones

- DRP/Protocol
- Prevalidation
 - protocol demo
 - multi-chem study
- Validation (inter-lab)

Current Status

- proj. Dec 04
- future
- future
- future

Mysid Lifecycle (Tier II)

aka Invertebrate Chronic

Milestones

- DRP/Protocol
- Prevalidation
 - protocol demo
 - multi-chem study
- Validation (inter-lab)

Current Status

✓ July 02

Proj. Dec 03

future

future

Fish Lifecycle (Tier II)

aka Fish Chronic

<u>Milestones</u>	<u>Current Status</u>
• DRP/Protocol	✓ Dec 02
• Prevalidation	
-protocol demo	future
-multi-chem study	future
• Validation (inter-lab)	future

August 19-21, 2003

- Fish Screen
 - Comparative FHM assays
 - comparative vitellogenin **Medaka, Zebrafish, FHM**
- Aromatase
- Steroidogenesis
- Pubertals male and female
- Strain / Species Discussion

Oct 2003

- Avian DRP
- In Utero through lactation protocol demonstration results

Spring 2004

- Amphibian Dev. & Repro. DRP (Tier II)
- Avian Dosing Study
- Amphibian Screen transferable protocol
- Fish Screen multi-chemical results
- Fish Screen Phase 1B (OECD)

